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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/903,508	07/13/2001	Charles Abbas	1533.0830003/MAC/RGM	3856

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STERNE, KESSLER, GOLDSTEIN & FOX PLLC
1100 NEW YORK AVENUE, N.W.
WASHINGTON, DC 20005

EXAMINER	
LAMBERTSON, DAVID A	

ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 02/13/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/903,508	ABBAS ET AL.	
	Examiner	Art Unit	
	David A. Lambertson	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 November 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-31* is/are pending in the application.

4a) Of the above claim(s) *22-31* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3,6,13 and 15-20* is/are rejected.

7)☒ Claim(s) *2,4,5,7-12,14 and 21* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Receipt is acknowledged of a reply to the previous Office Action, filed November 17, 2003. Amendments were made to the claims.

Claims 1-31 are pending in the instant application. Claims 22-31 are withdrawn as being drawn to a non-elected invention, as is the consideration of SEQ ID NO: 1 and 2. Claims 1-21 are under consideration in the instant application, with regard to the elected sequence SEQ ID NO: 3 only. Any rejection of record in the previous Office Action, mailed June 30, 2003, that is not addressed in this action has been withdrawn.

Because this Office Action only maintains rejections set forth in the previous Office Action and/or sets forth new rejections that are necessitated by amendment, this Office Action is made FINAL.

Claim Objections

Claims 1-14, 20 and 21 are objected to because of the following informalities: the claims refer to non-elected subject matter, specifically SEQ ID NOS: 1 and 2. Appropriate correction is required.

Applicant's response indicates a desire to postpone the cancellation of the non-elected subject matter, specifically SEQ ID NOS: 1 and 2, at the present time in order to await an indication of allowable subject matter, followed by rejoinder or linking claim practice. In response to this request, Applicant is respectfully notified that neither linking claim practice nor rejoinder is applicable in the instant case.

Regarding linking claim practice, there was no indication that linking claim practice was in effect in the Restriction/Election requirement mailed December 17, 2002. Furthermore, it was clearly indicated in the restriction requirement that the individual sequences are distinct inventions (i.e., distinct products), and that the Commissioner has indicated an election of a single sequence to be acceptable for examination in an application. It was further indicated that this was not a species election, and that one and only one sequence will be examined in the application.

With regard to rejoinder practice, rejoinder is in effect regarding a product and method of making and/or using said product. In the instant case, the different sequences claimed by applicant represent patentably distinct products, and not product and process of making and/or using claims. As a result, the distinct products are not subject to rejoinder, especially in light of the fact that the Commissioner has waived 37 CFR § 1.141 and indicated an election of a single nucleotide sequence to be appropriate for examination in a single application.

Miscellaneous

With regard to the rejection of claims 11-12 with regard to the biological deposit of ATCC-9058 and NRRL Y-30292, applicant has a provided a showing that the strains were commercially available. With regard to NRRL Y-30292, applicant has further indicated that any and all restrictions will be irrevocably removed regarding the availability of the strain for the life of the patent.

In regard to this manner, Applicant is respectfully pointed to MPEP § 2404.01 as it regards the implications of relying on a showing of public knowledge and availability of

Biological Materials. Although the MPEP indicates that it is improper to base a rejection under 35 USC 112, first paragraph on the mere prospect of a cessation in the public availability of a biological material, the MPEP also stresses the importance of making a deposit in order to satisfy the requirements of 35 USC 112, first paragraph. Specifically, the MPEP states that, "Public access may affect the enforceability of a patent...If an applicant has adequately established that a biological material is known and readily available, the Office will accept that showing. In those instances, however, the applicant takes the risk that the material may cease to be known and readily available. Such a defect cannot be cured by reissue after the grant of a patent."

In the instant case, the Examiner has decided to withdraw the rejection of claims 11-12 regarding the deposit of biological materials. However, as a courtesy, Applicant is advised of the risks taken regarding the reliance on a showing of public knowledge and availability of the biological materials, and is urged to make the biological deposit in order to ensure the enforceability of the patent for its life.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Rejections Necessitated by Amendment

Claim 19 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that

the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection. **This is a new rejection that is necessitated by the amendments to the claim.**

Claim 19 has been amended to contain the limitation "wherein said cell suspension comprises 0.3M to 1.0 M sucrose." Applicant points to various paragraphs in the specification that allegedly support the claimed range of sucrose concentrations. However, an examination of the specification, with particular attention paid to the indicated paragraphs, does not indicate a disclosure of the limitation "wherein said cell suspension comprises 0.3M to 1.0 M sucrose." There is no explicit or implicit description of the use of that particular range of sucrose concentrations (0.3M to 1.0 M) in the specification; therefore the limitation represents new matter.

Maintained Rejections

Claims 1, 3, 6, 13 and 20 stand rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. **This rejection is maintained for the reasons set forth in the previous Office Action.**

Claims 15-19 stand rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of electroporation of *Candida famata*, does not

reasonably provide enablement for a method of electroporation of any type of yeast. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. **This rejection is maintained for the reasons set forth in the previous Office Action.**

Response to Arguments Concerning Claim Rejections - 35 USC § 112

Applicant's arguments filed November 17, 2003 have been fully considered but they are not persuasive. With regard to the rejection of claims 1, 3, 6, 13 and 20, Applicant provides the following arguments:

1. The reference used in support of the rejection, Clyne *et al.*, is merely stating the activity found under the yeast transformation assay described in the article, and sequence similarities were reviewed in detail (see page 20 of Applicant's response, bottom paragraph).

2. According to the reference used in support of the rejection, ARS elements can be readily be identified on the basis of transformation frequency (see page 21 of Applicants response, top paragraph).

3. Applicant asserts that that the disclosure of two distinct yeast species having ARS elements, in conjunction with Applicants disclosure regarding ARS elements in C. *famata*, provides adequate written description of the claimed genus of ARS sequences having 95% sequence similarity to SEQ ID NO: 3.

4. SEQ ID NO: 3, by disclosing a nucleic acid sequence, provides the necessary structural features of an ARS sequence to allow the skilled artisan to envision the broad genus of claimed ARS sequences (i.e., those having 95% similarity to SEQ ID NO: 3).

Applicant's arguments are not found convincing for the following reasons:

1. Applicant's assessment of the teachings of Clyne is incomplete with regard to the outstanding rejection. The rejection of the instant claims is predicated on the percent homology (95%) that is claimed with regard to SEQ ID NO: 3, and the ability of sequences with 95% homology to SEQ ID NO: 3 to function as an ARS. In order to establish possession of the claimed genus, one of skill in the art would need to envision what 5% of SEQ ID NO: 3 could be altered while still retaining an ability to function as an ARS element. In order to envision such sequences, the skilled artisan would need to know what elements of the ARS sequence are absolutely required for functionality as an ARS element. The purpose of the Clyne reference is to establish the unreliability of relying simply on sequence homology to establish the ability of a sequence to function as an ARS.

The Clyne reference specifically states, "Although there are general similarities in the organization of ARS elements in budding and fission yeasts, ARS elements form one yeast are generally inactive in the other using this assay. This fact presumably reflects the differences in the proteins required for initiation of DNA replication and the origin sequences that they recognize. While there are similarities between the essential sequence elements of different *S. pombe* ARS elements, no strictly conserved sequences comparable to the budding yeast ACS is common to all such elements." Thus, the teachings of Clyne refer to the non-conserved nature of ARS sequence elements which are required for function, and establishes that a comparison of known ARS sequences is ineffective to envision the ability of a given ARS to function properly; this is because there are relatively few elements of common sequence among even the most well

characterized ARS elements (those of *S. pombe* and *S. cerevisiae*). With relatively few common elements of functionality among the best characterized ARS elements, it would be impossible for the skilled artisan to envision what 5% of the instantly claimed SEQ ID NO: 3 could effectively be changed while retaining the functional capacity of an ARS element without some further description of such elements in the instant specification. For instance, and as suggested by Clyne, an alteration in SEQ ID NO: 3 may adversely affect the ability of the proteins required for initiation and replication to bind to the ARS, thereby prohibiting the element to function properly as an ARS element. Without teachings of where the ARS element must remain unchanged for functionality, there can be no description of a sequence with 95% homology to SEQ ID NO: 3 which retains the ability to function as an ARS element.

The purpose of the Clyne reference is to establish what teachings are required in order to change up to 5% of SEQ ID NO: 3 while retaining ARS function. Clyne establishes that the skilled artisan would require some description of the elements that are necessary for the binding of proteins that are necessary for initiation and replication, at a minimum. Clyne further indicates that simple sequence comparison cannot establish this because of the limited conservation of common elements among well-known ARS elements. Because the specification does not teach what 5% of SEQ ID NO: 3 can be changed while retaining the ARS function of the sequence by demonstrating the functional portions of the sequence, and because the prior art indicates the inability to establish this by sequence comparison, the skilled artisan cannot reasonably envision what sequences having 95% similarity to SEQ ID NO: 3 have the ability to function as an ARS element.

2. The fact that ARS sequences can be identified has nothing to do with the *description* of these sequences. Applicant is claiming sequences having 95% homology to SEQ ID NO: 3, each of which must function as an ARS element. If these sequences are yet to be identified, they cannot be described. Since the sequences are not described, and cannot be envisioned by the skilled artisan in a reliable manner, the written description requirement for these sequences is not satisfied.

3. Applicant's assertion that the description of ARS elements in other yeast species (*S. pombe* and *S. cerevisiae*) provides a written description for the instantly claimed sequences is in direct contrast to the teachings of Clyne. As established above, Clyne indicates that determining the ability of an ARS element to properly function based upon sequence homology across species is unreliable at best. This, of course, is due to the lack of sequence similarity between common functional elements among the ARS elements of different species. Therefore, the skilled artisan cannot rely solely upon the sequence comparison of ARS elements from *S. pombe* and *S. cerevisiae* and the instantly claimed SEQ ID NO: 3 (from *C. famata*) to describe the instantly claimed invention because there is little-to-no conservation of the elements that are required for functionality. As a result, Applicant's assertion that the description of ARS elements in different species adequately describes sequences having 95% similarity to SEQ ID NO: 3 is not persuasive.

4. SEQ ID NO: 3, while describing a nucleic acid that is functional as an ARS element, does not describe those sequence elements that are absolutely necessary for its function as an ARS element. As a result, it does not describe the 5% of the sequence that can be changed while retaining the function of an ARS element. Furthermore, there is no indication or teaching in the

specification that establishes those sequences within SEQ ID NO: 3 that represent a structure-function relationship (i.e., what sequences are required for its function as an ARS element). Coupled with the teachings of Clyne, which indicate that simple sequence homology among ARS elements is insufficient to establish a structure-function relationship, Applicant has not described the broad genus of sequences that represent an ARS sequences with 95% homology to SEQ ID NO: 3.

In conclusion, while a sufficient written description is present for the ARS element SEQ ID NO: 3, there is not a sufficient written description for sequences having 95% homology to SEQ ID NO: 3 which retain an ARS function. This is because the specification does not describe the particular sequences within SEQ ID NO: 3 that provide a structure-function relationship, and the prior art establishes that it is not possible to rely on sequence homology with other ARS elements to establish regions of structure-function due to a lack of commonality between ARS elements. Therefore, the skilled artisan cannot envision the broad genus of claimed sequences because the skilled artisan cannot ascertain where alterations in SEQ ID NO: 3 can or cannot be made while retaining the functionality of the ARS element. As a result, the written description requirement for the broadly claimed genus of ARS elements having 95% homology to SEQ ID NO: 3 is not satisfied, and the previous rejection is maintained.

Applicant's arguments filed November 17, 2003 have been fully considered but they are not persuasive. With regard to the enablement rejection, Applicant presents the following arguments:

1. Applicant disagrees with the assertion that the applicability of the 8-15 kV/cm field strength is only enabling for a method of electroporating *Candida famata*, suggesting that the supportive reference (the '309 patent) is only one body of references regarding field strengths that can be used for electroporating various yeasts (see page 23-24 of Applicant's arguments).

2. Applicant cites a number of references discussing the parameters of field strength with regard to electroporation of divergent yeast strains, in what appears to be an attempt to support the notion that a field strength of 8-15 kV/cm can be used to electroporate any yeast strain.

Applicant's arguments are not convincing for the following reasons:

1 and 2. Applicant suggests that the '309 patent is not a representation of the electroporation conditions that can be used with yeast cells. However, the references that Applicant cites only serve to support the assertion that conditions of electroporation that require a field strength of 8-15 kV/cm are unpredictable for use with yeast cells that are not *Candida famata*. For instance, the Becker and Guarente reference indicates using a field strength of 7.5 kV/cm to transform *S. cerevisiae*, and various references do not even disclose a field strength (i.e., the Pia *et al.* and Scorer *et al.* references). None of these references indicate that the claimed field strength of 8-15 kV/cm can be used to transform any yeast cell types because none of them show the applicability of such a field strength to any yeast type. Rather, the disclosures of theses references support the assertion that using such a field strength is unpredictable with regard to yeast cells other than *Candida famata*, because the transformation of these yeast strains makes use of field strengths that are below the instantly claimed field strength. As such, the '309 patent is not the only body of evidence that questions the applicability of a field strength of 8-15kV/cm to any yeast strain.

In conclusion, the instant specification only makes use of these particular field strengths (8-15 kV/cm) for the electroporation of *Candida famata* cells, and does not clearly indicate the applicability of such field strengths to other types of yeast cells. The prior art does not remedy this because the ideal field strengths used in the electroporation of other types of yeast cells, such as the '309 patent (2.54-4.5 kV/cm field strength) and the Becker and Guarente reference (field strength of 7.5 kV/cm), are below the field strengths claimed in the instant claims. As a result of these teachings, the skilled artisan would have to practice undue trial and error experimentation in order to empirically determine what types of yeast cells could be electroporated at elevated field strengths, such as those in the instant claims. Since this empirical experimentation is at the heart of the invention, the claims merely represent an invitation to experimentation. As a result, the claims are not found to be enabled over the broad scope in which it is claimed.

Allowable Subject Matter

Claims 2, 4, 5, 7-12, 14 ad 21 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Claims 1-14, 20 and 21 are objected to as containing subject matter which is non-elected by original presentation.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David A. Lambertson whose telephone number is (571) 272-0771. The examiner can normally be reached on 6:30am to 4pm, Mon.-Fri., first Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel, Ph.D. can be reached on (571) 272-0781. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

David A. Lambertson, Ph. D.
AU 1636

JAMES KETTER
PRIMARY EXAMINER